UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,774	03/26/2001	Sunghwa Choe	2225-0020	7797

26191 7590 11/05/2003

FISH & RICHARDSON P.C.
3300 DAIN RAUSCHER PLAZA
60 SOUTH SIXTH STREET
MINNEAPOLIS, MN 55402

EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,774	CHOE ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on th cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-77* is/are pending in the application.

4a) Of the above claim(s) *46,47,55 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-45,48-54 and 57-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/26/01, 8/18/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. The amendment filed 8/18/2003 has been entered.

2. Claims 40-77 are pending.

   Claims 1-39 have been canceled.

   Newly submitted claims 40-77 are not drawn to a single invention.

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 40-45, 48-54, 57-77 are drawn to an isolated nucleotide sequence of SEQ ID NO:30 encoding a sterol delta-7 reductase polypeptide of SEQ ID NO:31, and transgenic plant transformed therewith, classified in class 800, subclass 278 for example.

   II. Claims 46-47, 55-56, are drawn to an isolated nucleotide sequence of SEQ ID NO:28 encoding a SEQ ID NO:29, classified in class 536, subclass 23.6 for example.

4. Inventions I and II are unrelated to each other because nucleotide sequences either encoding different proteins or specifying specific expression patterns are structurally distinct chemical compounds and are unrelated to one another, as are different proteins structurally distinct chemical compounds and unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR

1.141 et seq (see MPEP 803.04 and 2434). This requirement is not to be construed as a requirement for an election of species, since each nucleotide and amino acid sequence is not a member of a single genus of invention, but constitutes an independent and patentably distinct invention.

5. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the literature and sequence searches required for each of the Groups are not required for another of the Groups, restriction for examination purposes as indicated is proper.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

7. Newly submitted claims 46-47 and 55-56 are directed to an invention that is independent or distinct from the invention originally claimed for the reasons set forth above.

8. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 46-47 and 55-56 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

9. Claims 40-45, 48-54, 57-77 are examined in the present office action.

10. Rejections and objections not set forth below are withdrawn.

11. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

Claim Objections

12. Claims 48, and 49 are objected to for being dependent on non-elected inventions. Correction is required.

New Matter

13. Claims 41-45, 64-71, and 77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 41-45, and 64-66 are drawn to an isolated nucleic acid comprising a nucleotide sequence encoding any sterol delta-7 reductase polypeptide, wherein said nucleotide sequence has a mutation, wherein the mutation can be a deletion, insertion, substitution or a substitution and insertion, or wherein the substitution and insertion introduce 44 amino acids into the encoded polypeptide, a sterol delta-7 reductase coding sequence of claim 57, wherein the polypeptide encoded by said sequence is defective for catalyzing the sterol delta-7 reduction of episterol to 24-methylenecholesterol and campesterol, or where the transgenic plant comprising the sequence of claim 57 is more effective at converting episterol to C-7-dehydrocampesterol, or said plant is more effective at converting episterol to C-7-dehydrocampestanol, all of which,

when compared to a plant expressing a wild type sterol delta-7 reductase coding sequence. The before mentioned claimed inventions do not have support in the presently filed application and are considered new matter.

Indefiniteness

14. Claims 40-45, 50-54, and 57-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Rejection includes dependent claims.

In claims 40 and 57, the metes and bounds of a "mixed charge cluster domain" have not been defined. It is unclear what is encompassed in Applicants' "mixed charge cluster domain". Applicants have not defined the biochemical components of a "mixed charge cluster domain".

In claims 42, 43, 44, and 45, 1st line, replace "introduces" with --results in--, to further clarify Applicant's claimed invention.

In claim 45, it is unclear whether "44 amino acids" also applies to the "substitution".

In claim 64, the metes and bounds of "defective" have not been defined. It is unclear if "defective" refers to the inability of the sterol delta-7 reductase to catalyze any reactions or if the enzyme catalyzes the reaction at a slower rate or level, when compared to wild type.

In claim 65, the metes and bounds of "more effective" have not been defined. Does "more effective" refer to the rate or level of the specified enzymatic activity? All subsequent recitations of "more effective" are also rejected.

Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP

§ 2172.01. In any of claims 52, 61, 65, 66, 69, and 74, Applicant has not specified that the claimed sequence is "expressed". Without "expression" of the claimed nucleic acid, the claimed characteristics will not occur.

Written Description

15. Claims 40-45, 50-54, 57, and 59-77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid comprising a nucleotide sequence encoding any sterol delta-7 reductase polypeptide, wherein said nucleotide sequence has a mutation, wherein the mutation can be a deletion, insertion, substitution or a substitution and insertion, or wherein the substitution and insertion introduce 44 amino acids into the encoded polypeptide, or wherein a control element is operably linked to any of the above mentioned sequences and host cell or plant transformed therewith, or a method of producing a transgenic plant comprising transforming a plant with an above sequence.

Applicants isolated their invention by creating a mapping F2 population by crossing *dwf5-1* to Columbia wild type and selecting 50 different dwarf plants from the F2 population. Using primers DW5_3F and DW5_LR, DNA was amplified and then sequenced (page 52, 1st paragraph). Applicants do not disclose any specific structural, physical and/or chemical properties for the claimed sequence. Applicants do not present a description of domains that are specific to this particular sterol delta-7 reductase (S7R) nor domains that are important for its proper function. The claims encompass mutants and allelic variants and thus imply that

structural variants exist in nature, yet no structural variant has been disclosed. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known. Therefore, there is insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine which sequences exhibiting the claimed limitations would function as a sterol delta-7 reductase polynucleotide or to determine mutants and allelic variants from other plants and organisms absent further guidance. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention. (See Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Applicants contend that because original claims 1-8, 10, 14-16 and 18-21 have been canceled, the written description rejection is moot.

The Office contends that the written description requirements are not fulfilled for the newly submitted set of claims.

Enablement

16. Claims 40-45, 48-54, 57-77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number

of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated nucleic acid comprising a nucleotide sequence encoding any sterol delta-7 reductase polypeptide, wherein said nucleotide sequence has a mutation, wherein the mutation can be a deletion, insertion, substitution or a substitution and insertion, or wherein the substitution and insertion introduce 44 amino acids into the encoded polypeptide, or wherein a control element is operably linked to any of the above mentioned sequences and host cell or plant transformed therewith, or a method of producing a transgenic plant comprising transforming a plant with an above sequence.

Applicants' invention is SEQ ID NO:30 (*dwf5-1*) encoding a mutant sterol delta-7 reductase of SEQ ID NO:31. The *dwf5-1* mutant was isolated from a mutagensis screen of *Arabidopsis* plants that had been mutagenized by T-DNA insertion. Applicants have not reduced to practice their invention. They have only described the cloning and characterization of *dwf5-1* mutant and corresponding nucleic acid sequence and they have also shown that ectopic over-expression of the *DWF5* cDNA in *dwf5-1* mutants completely converts the mutants to wild-type plants (page 63, lines 9-11).

Applicants have not taught how one skilled in the art would use plants transformed with SEQ ID NO:30 nor have Applicants taught how one skilled in the art would use SEQ ID NO:30

to generate a specific agronomically important plant. Applicants teach the importance of sterol delta-7 reductase in plant developmental and physiological processes but Applicants have not specifically addressed how an isolated nucleic acid encoding a mutant sterol delta-7 reductase polypeptide, wherein the mutant polypeptide comprises a deletion, insertion, substitution or substitution and insertion or wherein the substitution and insertion comprises an insertion of 44 amino acids, all of which can be used in a plant to achieve a specific phenotype or biological process. Applicants have also not taught what kind of mutation is required and where the mutation should be located, to either retain endogenous activity or create a polypeptide that is either defective or more effective at producing the claimed reactions. In addition, how would one use the specified polynucleotides to produce a plant having a specific phenotype. It has not been taught how transforming a plant with an above mentioned sequence will produce a dominant phenotype that over-rides the wild-type activity of the endogenous polypeptide.

It cannot be predicted by one of skill in the art that nucleic acids comprising a mutation, wherein the mutation can be a deletion, insertion, substitution or a substitution and insertion, or wherein the substitution and insertion introduce 44 amino acids into the encoded polypeptide, will encode a protein with a different activity as the wild-type protein. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many

amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants. In the present application, the *dwf5-1* allele has a single base pair deletion and renders the corresponding protein inactive (page 53, Table 2).

The state-of-the-art teaches heterologous nucleic acid molecules encoding enzymes involved in biochemical pathways does not always produce the expected results. Hamada et al (1998, Plant Physiology 118:591-598) teach that expressing heterologous desaturases in plants does not always give predictable results. Hamada et al overexpressed a tobacco microsomal ω-3 fatty acid desaturase cDNA (NtFAD3) under the control of a mosaic constitutive promoter that confers about 10-fold higher levels of constitutive expression than the CaMV 35S promoter. The results of overexpression in tobacco plants resulted in a 40% increase in alpha-linolenic acid in roots and only a 10% increase in leaves (abstract and page 593, right column, 1st paragraph of

results). These results suggest that endogenous factors contribute to the observed result that can not be predicted a priori.

Therefore, given the unpredictability of using heterologous nucleic acids to alter the normal synthesis of biochemical macro-molecules for the reasons stated above; given the lack of guidance and examples of how one would use a plant transformed with a nucleic acid encoding a mutant sterol delta-7 reductase polypeptide, or how one would use a nucleic acid encoding a mutant sterol delta-7 reductase polypeptide to generate a plant with a specific phenotype or for a specific purpose; for the reason stated above; given the breath of the claims that encompass any mutant comprising any insertion, deletion, substitution of any size or substitution and insertion comprising 44 amino acids; and given the state-of-the-art as discussed above, undue experimentation would be required by one skilled in the art to make and/or use the broadly claimed invention.

Applicants contend that because original claims 1-8, 10, 14-16 and 18-21 have been canceled, the enablement rejection is moot.

The Office contends that Applicants have not enabled the newly submitted claims for the reasons set forth above.

Non-Statutory Utility Rejection

17. Claims 53, 62, 70, and 75 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 53, 62, 70, and 75 are drawn to a seed of the transformed plant. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be

transferred at most to half the male gametes and half the female gametes. This translates into three quarters of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Given that there is no indication that there would be any other distinguishable characteristics of the claimed progeny (seeds), it is unclear whether the claimed seeds would be distinguishable from seeds that would occur in nature. See *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 76 USPQ 280 (1948), and *In re Bergy , Coats, and Malik* 195 USPQ 344, (CCPA) 1977. The amendment of the claims to recite that the seeds comprise the construct that was introduced into the parent seed would overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claims 40-45, 50-54, 57, and 59-77 are rejected under 35 U.S.C. 102(e) as being anticipated by Famodu et al (102(e) date of November 1998, U.S. Patent Number 6,465,717).

The claims are drawn to an isolated nucleic acid comprising a nucleotide sequence encoding any sterol delta-7 reductase polypeptide, wherein said nucleotide sequence has a mutation, wherein the mutation can be a deletion, insertion, substitution or a substitution and insertion, or wherein the substitution and insertion introduce 44 amino acids into the encoded

polypeptide, or wherein a control element is operably linked to any of the above mentioned sequences and host cell or plant transformed therewith, or a method of producing a transgenic plant comprising transforming a plant with an above sequence. The claims are also drawn to any sterol delta-7 reductase polypeptide comprising a mutation, wherein the mutation can be a deletion, insertion, substitution or a substitution and insertion, or wherein the substitution and insertion introduce 44 amino acids into the encoded polypeptide, a sterol delta-7 reductase coding sequence of claim 57, wherein the polypeptide encoded by said sequence is defective for catalyzing the sterol delta-7 reduction of episterol to 24-methylenecholesterol and campesterol, or where the transgenic plant comprising the sequence of claim 57 is more effective at converting episterol to C-7-dehydrocampesterol, or said plant is more effective at converting episterol to C-7-dehydrocampestanol, all of which, when compared to a plant expressing a wild type sterol delta-7 reductase coding sequence.

Famodu et al teach an isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide having sterol delta-7 reductase activity, wherein the amino acid sequence of the polypeptide and the amino acid sequence of Famodu et al's SEQ ID NO:20 have at least 85% sequence identity, or a recombinant DNA construct comprising the above sequence operably linked to at least one regulatory sequence, a plant cell and plant transformed with said recombinant DNA construct and a method for producing a transgenic plant comprising transforming a plant with said recombinant DNA construct, and Famodu et al also claim a seed comprising said recombinant DNA construct. The invention of Famodu et al encompass Applicants' claims drawn to any mutant sequence as recited by Applicants and it would be an inherent property of Famodu et al's claimed sequences to encode a polypeptide that is defective

for catalyzing the sterol delta-7 reduction of episterol to 24-methylenecholesterol and campesterol, or wherein the transgenic plants of Famodu et al comprise a sequence that is more effective at converting episterol to C-7-dehydrocampesterol, or is more effective at converting episterol to C-7-dehydrocampestanol, all of which, when compared to a plant expressing a wild type sterol delta-7 reductase coding sequence, and as such, Famodu et al anticipate the claimed invention.

19. Claims 48-49, and 58 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:30 encoding SEQ ID NO:31.

20. No claims are allowed.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 703-305-6997. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Stuart F. Baum Ph.D.

November 3, 2003

Phuong Bui 11/3/03

PHUONG T. BUI
PRIMARY EXAMINER